Use of Atypical Antipsychotics in the Elderly

by Elisa Cascade; Amir H. Kalali, MD; and Jeffrey L. Cummings, MD

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ABSTRACT: Recent research on dementia patients suggests that use of antipsychotics may increase risk of hospitalization or death. While bipolar disorder and schizophrenia combine to represent more than 70 percent of atypical antipsychotic uses in younger patients, these same indications represent only 38 percent of product use in patients age 65 and older. The difference between the two age groups is driven primarily by use in cognitive impairment: Dementia and Alzheimer's combine to account for 28 percent of atypical antipsychotic use in older patients. Although ICD-9 coding tends to group patients into less specific diagnoses, we did isolate a small group of approximately 10 percent of patients that were classified based on the presence or absence of behavior disturbances. Eighteen percent of dementia patients without behavioral disturbances received atypical antipsychotics as compared to 66 percent of patients with behavioral disturbances. A discussion of the results is provided.

KEY WORDS: Alzheimer's, dementia, antipsychotics

INTRODUCTION

Recent research on dementia patients suggests that use of antipsychotics may increase risk of hospitalization or death. In this article, we examine prevalence of atypical antipsychotic use in patients over the age of 65 and reasons for product use.

METHODS

We obtained data from two different sources: 1) patients taking atypical antipsychotics from Verispan's Total Patient Tracker, May, 2007, to April, 2008, and 2)

May, 2007, to April, 2008, data from Verispan's Prescription Drug and Diagnosis Audit (PDDA) regarding reasons for use of atypical antipsychotics. PDDA captures data on disease state and associated therapy from 3,100 office-based physicians representing 29 specialties across the United States.

RESULTS

Over the past year, 5.5 million Americans filled at least one prescription for an atypical antipsychotic; 19 percent of whom (approximately 1 million) were age 65 and older. Figure 1 displays reasons for use of atypical antipsychotics in patients under age 65 and age 65 and older. As seen in Figure 1, while bipolar disorder and schizophrenia combine to represent over 70 percent of atypical antipsychotic uses in younger patients, these same indications represent only 38 percent of product use in older patients. The difference between the two age groups is driven primarily by the additional 28 percent of use among patients with cognitive impairment (dementia and Alzheimer's combined).

We examined the data further to determine whether there were differences in use of atypical antipsychotics by dementia patients with and without and behavioral disturbances. Although ICD-9 coding tends to group patients into less specific diagnoses, we did isolate a small group of approximately 10 percent of patients who were classified based on the presence or absence of behavioral disturbances. Figure 2 displays the prevalence of atypical antipsychotic use among these patient groups. As seen in Figure 2, 18 percent of dementia patients without behavioral disturbances received atypical antipsychotics as compared to 66 percent of patients with behavioral disturbances.

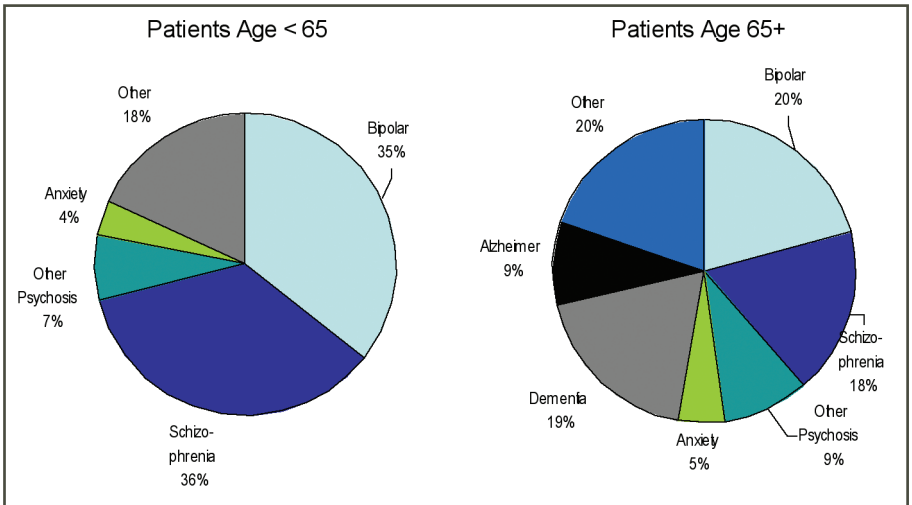

FIGURE 1. Reasons for use of atypical antipsychotics by patient age
Source: Verispan PDDA, Atypical Antipsychotics May 2007 to April 2008.

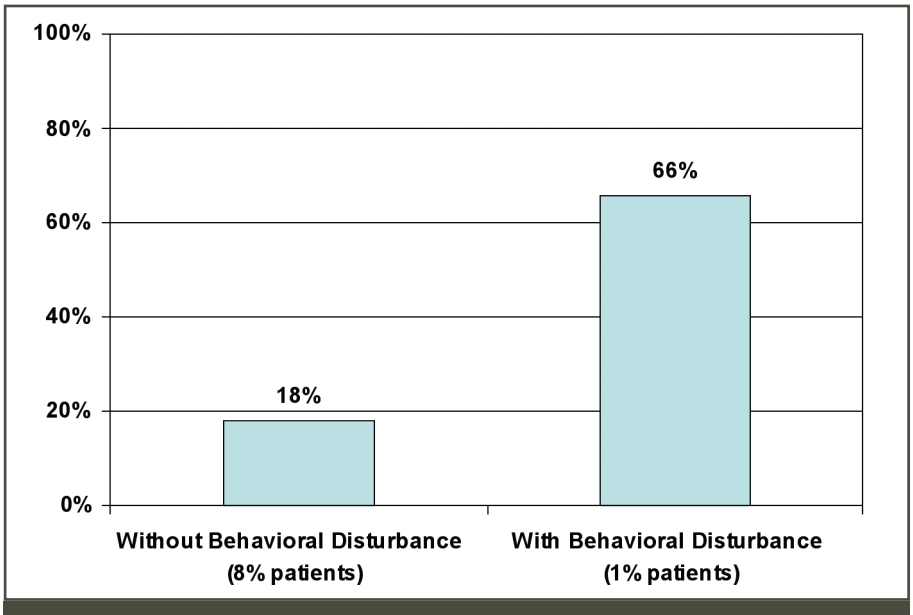

FIGURE 2. Proportion of Alzheimer's disease patients receiving antipsychotics
Source: Verispan PDDA, ICD-9 Diagnosis 294.10 (without behavioral disturbance) and 294.11 (with behavioral disturbance), May 2007 to April 2008

COMMENTARY

by Jeffrey L. Cummings

This article focuses on an area of continuing unmet need in the elderly population: agents that effectively treat behavioral disturbances in elderly patients without compromising safety. All current atypical antipsychotics carry a "black box" type of warning required by the Food and Drug Administration (FDA), indicating

that these agents have been associated with an increased risk of mortality in the elderly. The label asserts the following: Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5 percent, compared to a rate of about 2.6 percent in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature.

Note that the exposures were for 10 weeks and it is uncertain from the available data if more deaths are to be expected with longer exposures or if patients at risk express their vulnerabilities early and succumb soon after exposure. The absolute risk remains small (4.5% compared to the placebo rate of 2.6%) but the relative risk—an almost two-fold increase—is not trivial. Also uncertain from the available data is the mechanism by which mortality is exacerbated, although even mild drug-induced parkinsonism with attendant immobility and swallowing difficulties may contribute to the elevated rates of pneumonia reported among elderly patients receiving atypical agents.[1] Not all analyses of the data have supported the conclusions drawn by the FDA, but an analysis by Schneider, et al.,[2] came to nearly identical conclusions.

Although the mortality warning is mandated only for atypical antipsychotics, similar increases in death rates have been identified among dementia patients treated with conventional neuroleptic agents.[3,4]

The warning on atypicals and the concern over conventional neuroleptics has created tremendous uncertainty in the prescribing community. The safety concerns are heightened by recent studies raising serious questions about the effectiveness of these agents as currently used in clinical practice. They are often given in doses that are too low for periods of time that are too short to draw therapeutic conclusions, thus possibly exposing patients to the risks while not providing the putative benefits of these agents.[5]

There are no therapies approved by the FDA for treatment of behavioral disturbances in dementia, and alternative medications, such as mood-stabilizing anticonvulsants, have lacked efficacy in recent randomized, controlled trials.[6,7] Antidementia drugs, such as memantine, may have anti-agitation effects,[8] but many patients develop treatment-requiring behavioral syndromes despite treatment with these drugs. Thus, clinicians are faced with the dilemma that the most common behavioral disturbance in dementia for which medications are needed has no satisfactory treatment. Antipsychotics are used because they have been shown in some trials to be efficacious and because the clinician has few if any viable options.[9–11]

Not treating psychosis and agitation in dementia patients may also have consequences: injury to patient and spouse, premature institutionalization, and use of restraints, among others. Thus, the decision to use these agents must be based on a dialogue between informed caregivers and patients and their physicians with candid discussions of data regarding efficacy and risks. A ban on use of these agents would be as inappropriate as their intemperate use. Figures 1 and 2 demonstrate that this is the course adopted by most current practitioners. The American College of Neuropsychopharmacology Work Group and a recent Best Practices Panel endorsed this approach in recent guidelines for use of atypicals in patients with dementia.[12,13]

The current situation is untenable. The rising number of elderly and the concomitant anticipated dramatic rise in the number of patients with dementia makes a marked increase in the number of elderly cognitively impaired persons requiring treatment for behavioral disturbances inevitable. Progress in understanding the neurobiology of Alzheimer's disease and enhanced understanding of the neurobiology of psychosis may lead to discovery of agents with psychotropic properties and safety profiles superior to those currently available.[14]

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